

WHAT IS CLAIMED

1. ~~An isolated nucleic acid molecule comprising~~
a nucleotide sequence selected from the group
5 consisting of:

(a) the nucleotide sequence set forth in SEQ
ID NO: 2;

B2 (b) a nucleotide sequence encoding the
polypeptide set forth in SEQ ID NO: 1;

10 (c) a nucleotide sequence which hybridizes
under moderately or highly stringent conditions to the
complement of (a) or (b), wherein the encoded
polypeptide, when heterodimerized to human $\alpha 2$
polypeptide, has an activity of the human $\alpha 2/\beta 10$
15 heterodimer; and

(d) a nucleotide sequence complementary to
any of (a)-(c).

2. An isolated nucleic acid molecule comprising
20 a nucleotide sequence selected from the group
consisting of:

(a) a nucleotide sequence encoding a
polypeptide that is at least about 70, 75, 80, 85, 90,
95, 96, 97, 98, or 99 percent identical to the
25 polypeptide set forth in SEQ ID NO: 1, wherein the
polypeptide, when heterodimerized to human $\alpha 2$
polypeptide, has an activity of the human $\alpha 2/\beta 10$
heterodimer;

(b) a nucleotide sequence encoding an
30 allelic variant or splice variant of the nucleotide
sequence set forth in SEQ ID NO: 2, wherein the encoded

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polypeptide, when heterodimerized to human $\alpha 2$ polypeptide, has an activity of the human $\alpha 2/\beta 10$ heterodimer;

- 5 (c) a nucleotide sequence of SEQ ID NO: 2, (a), or (b) encoding a polypeptide fragment of at least about 25 amino acid residues, wherein the polypeptide, when heterodimerized to human $\alpha 2$ polypeptide, has an activity of the human $\alpha 2/\beta 10$ heterodimer;

- 10 (d) a nucleotide sequence of SEQ ID NO: 2 or (a)-(c) comprising a fragment of at least about 16 nucleotides;

- 15 (e) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a)-(d), wherein the encoded polypeptide, when heterodimerized to human $\alpha 2$ polypeptide, has an activity of the human $\alpha 2/\beta 10$ heterodimer; and

- 20 (f) a nucleotide sequence complementary to any of (a)-(c).

3. An isolated nucleic acid molecule comprising a nucleotide sequence selected from the group consisting of:

- 25 (a) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 1 with at least one conservative amino acid substitution, wherein the polypeptide, when heterodimerized to human $\alpha 2$ polypeptide, has an activity of the human $\alpha 2/\beta 10$ heterodimer;

- 30 (b) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 1 with at least

one amino acid insertion, wherein the polypeptide, when heterodimerized to human $\alpha 2$ polypeptide, has an activity of the human $\alpha 2/\beta 10$ heterodimer;

5 (c) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 1 with at least one amino acid deletion, wherein the polypeptide, when heterodimerized to human $\alpha 2$ polypeptide, has an activity of the human $\alpha 2/\beta 10$ heterodimer;

10 (d) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 1 which has a C- and/or N- terminal truncation, wherein the polypeptide, when heterodimerized to human $\alpha 2$ polypeptide, has an activity of the human $\alpha 2/\beta 10$ heterodimer;

15 (e) a nucleotide sequence encoding a polypeptide as set forth in SEQ ID NO: 1 with at least one modification selected from the group consisting of amino acid substitutions, amino acid insertions, amino acid deletions, C-terminal truncation, and N-terminal truncation, wherein the polypeptide, when
20 heterodimerized to human $\alpha 2$ polypeptide, has an activity of the human $\alpha 2/\beta 10$ heterodimer;

(f) a nucleotide sequence of (a)-(e) comprising a fragment of at least about 16 nucleotides;

25 (g) a nucleotide sequence which hybridizes under moderately or highly stringent conditions to the complement of any of (a)-(f), wherein the encoded polypeptide, when heterodimerized to human $\alpha 2$ polypeptide, has an activity of the human $\alpha 2/\beta 10$ heterodimer; and

30 (h) a nucleotide sequence complementary to

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any of (a)-(e).

4. A vector comprising the nucleic acid molecule of Claims 1, 2, or 3.

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5. A host cell comprising the vector of Claim 4.

6. The host cell of Claim 5 that is a eukaryotic cell.

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7. The host cell of Claim 5 that is a prokaryotic cell.

8. A process of producing a β 10 polypeptide comprising culturing the host cell of Claim 5 under suitable conditions to express the polypeptide, and optionally isolating the polypeptide from the culture.

9. A polypeptide produced by the process of Claim 8.

10. The process of Claim 8, wherein the nucleic acid molecule comprises promoter DNA other than the promoter DNA for the native β 10 polypeptide operatively linked to the DNA encoding the β 10 polypeptide.

11. The isolated nucleic acid molecule according to Claim 2 wherein the percent identity is determined using a computer program selected from the group consisting of GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit, and the Smith-Waterman algorithm.

12. A process for determining whether a compound modulates β 10 polypeptide activity or production

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comprising exposing a cell comprising the vector of claim 4 to the compound, and measuring β 10 polypeptide activity or production in said cell.

5 13. An isolated polypeptide comprising the amino acid sequence set forth in SEQ ID NO: 3.

14. An isolated polypeptide comprising the amino acid sequence selected from the group consisting of:

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10 (a) the mature amino acid sequence as set forth in SEQ ID NO: 3, comprising a mature amino terminus at residue 1, optionally further comprising an amino-terminal methionine;

15 (b) an amino acid sequence for an ortholog of SEQ ID NO: 3, wherein the encoded polypeptide, when heterodimerized to human α 2 polypeptide, has an activity of the human α 2/ β 10 heterodimer;

20 (c) an amino acid sequence that is at least about 70, 75, 80, 85, 90, 95, 96, 97, 98, or 99 percent identical to the amino acid sequence of SEQ ID NO: 3, wherein the polypeptide, when heterodimerized to human α 2 polypeptide, has an activity of the human α 2/ β 10 heterodimer;

25 (d) a fragment of the amino acid sequence set forth in SEQ ID NO: 3 comprising at least about 25 amino acid residues, wherein the polypeptide, when heterodimerized to human α 2 polypeptide, has an activity of the human α 2/ β 10 heterodimer;

30 (e) an amino acid sequence for an allelic variant or splice variant of either the amino acid sequence set forth in SEQ ID NO: 3 or at least one of (a)-(c) wherein the polypeptide, when heterodimerized

to human $\alpha 2$ polypeptide, has an activity of the human $\alpha 2/\beta 10$ heterodimer.

15. An isolated polypeptide comprising the amino
5 acid sequence selected from the group consisting of:

(a) the amino acid sequence set forth in SEQ
ID NO: 3 with at least one conservative amino acid
substitution, wherein the polypeptide, when
heterodimerized to human $\alpha 2$ polypeptide, has an
10 activity of the human $\alpha 2/\beta 10$ heterodimer;

(b) the amino acid sequence set forth in SEQ
ID NO: 3 with at least one amino acid insertion,
wherein the polypeptide, when heterodimerized to human
 $\alpha 2$ polypeptide, has an activity of the human $\alpha 2/\beta 10$
15 heterodimer;

(c) the amino acid sequence set forth in SEQ
ID NO: 3 with at least one amino acid deletion, wherein
the polypeptide, when heterodimerized to human $\alpha 2$
polypeptide, has an activity of the human $\alpha 2/\beta 10$
20 heterodimer;

(d) the amino acid sequence set forth in SEQ
ID NO: 3 which has a C- and/or N-terminal truncation,
wherein the polypeptide, when heterodimerized to human
 $\alpha 2$ polypeptide, has an activity of the human $\alpha 2/\beta 10$
25 heterodimer; and

(e) the amino acid sequence set forth in SEQ
ID NO: 3, with at least one modification selected from
the group consisting of amino acid substitutions, amino
acid insertions, amino acid deletions, C-terminal
30 truncation, and N-terminal truncation, wherein the
polypeptide, when heterodimerized to human $\alpha 2$

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polypeptide, has an activity of the human $\alpha 2/\beta 10$ heterodimer.

16. An isolated polypeptide encoded by the
5 nucleic acid molecule of Claims 1, 2, or 3.

17. The isolated polypeptide according to Claim
14 wherein the percent identity is determined using a
computer program selected from the group consisting of
10 GAP, BLASTP, BLASTN, FASTA, BLASTA, BLASTX, BestFit,
and the Smith-Waterman algorithm.

18. An antibody produced by immunizing an animal
with a peptide comprising the amino acid sequence of
15 SEQ ID NO: 3.

19. An antibody or fragment thereof that
specifically binds the polypeptide of Claims 13, 14, or
15.

20. The antibody of Claim 19 that is a monoclonal
antibody.

21. A hybridoma that produces a monoclonal
25 antibody that binds to a peptide comprising the amino
acid sequence of SEQ ID NO: 3.

22. A method of detecting or quantitating the
amount of $\beta 10$ polypeptide using an anti- $\beta 10$ antibody or
30 fragment thereof which specifically binds the
polypeptide of claims 13, 14 or 15.

23. A selective binding agent or fragment thereof
that specifically binds at least one polypeptide,
35 wherein said polypeptide comprises the amino acid

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sequence selected from the group consisting of:

(a) the amino acid sequence set forth in SEQ ID NO: 3; and

5 (b) a fragment of the amino acid sequence set forth in SEQ ID NO: 3; and

(c) a naturally occurring variant of (a) or (b).

10 24. The selective binding agent of Claim 23 that is an antibody or fragment thereof.

25. The selective binding agent of Claim 23 that is a humanized antibody.

15 26. The selective binding agent of Claim 23 that is a human antibody or fragment thereof.

20 27. The selective binding agent of Claim 23 that is a polyclonal antibody or fragment thereof.

28. The selective binding agent of Claim 23 that is a monoclonal antibody or fragment thereof.

25 29. The selective binding agent of Claim 23 that is a chimeric antibody or fragment thereof.

30. The selective binding agent of Claim 23 that is a CDR-grafted antibody or fragment thereof.

30 31. The selective binding agent of Claim 23 that is an anti-idiotypic antibody or fragment thereof.

32. The selective binding agent of Claim 23 which

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is a variable region fragment.

33. The variable region fragment of Claim 32 which is a Fab or a Fab' fragment.

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34. A selective binding agent or fragment thereof comprising at least one complementarity determining region with specificity for a polypeptide having the amino acid sequence of SEQ ID NO: 3.

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35. The selective binding agent of Claim 23 which is bound to a detectable label.

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36. The selective binding agent of Claim 23 which antagonizes β 10 polypeptide biological activity.

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37. A method for treating, preventing, or ameliorating a disease, condition, or disorder comprising administering to a patient an effective amount of a selective binding agent according to Claim 23.

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38. A method for treating, preventing, or ameliorating a thyroid gland related disease, condition, or disorder comprising administering to a patient an effective amount of a selective binding agent according to Claim 23.

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39. A selective binding agent produced by immunizing an animal with a polypeptide comprising the amino acid sequence of SEQ ID NO: 3.

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40. A hybridoma that produces a selective binding agent capable of binding a polypeptide according to Claims 1, 2, or 3.

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41. A composition comprising the polypeptide of Claims 13, 14, or 15 and a pharmaceutically acceptable formulation agent.

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42. The composition of Claim 41 wherein the pharmaceutically acceptable formulation agent is a carrier, adjuvant, solubilizer, stabilizer, or anti-oxidant.

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43. The composition of Claim 41 wherein the polypeptide comprises the mature amino acid sequence as set forth in SEQ ID NO: 3.

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44. A polypeptide comprising a derivative of the polypeptide of Claims 13, 14, or 15.

45. The polypeptide of Claim 44 which is covalently modified with a water-soluble polymer.

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46. The polypeptide of Claim 45 wherein the water-soluble polymer is selected from the group consisting of polyethylene glycol, monomethoxy-polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide copolymers, polyoxyethylated polyols, and polyvinyl alcohol.

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47. A composition comprising a nucleic acid molecule of Claims 1, 2, or 3 and a pharmaceutically acceptable formulation agent.

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48. A composition of Claim 47 wherein said nucleic acid molecule is contained in a viral vector.

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49. A viral vector comprising a nucleic acid molecule of Claims 1, 2, or 3.

5 50. A fusion polypeptide comprising the polypeptide of Claims 13, 14, or 15 fused to a heterologous amino acid sequence.

51. The fusion polypeptide of Claim 50 wherein
10 the heterologous amino acid sequence is an IgG constant domain or fragment thereof.

52. A method for treating, preventing or ameliorating a medical condition comprising
15 administering to a patient the polypeptide of Claims 13, 14, or 15 or the polypeptide encoded by the nucleic acid of Claims 1, 2, or 3.

53. A method of diagnosing a pathological
20 condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of Claims 13, 14, or 15 or the polypeptide encoded by the nucleic acid molecule
25 of Claims 1, 2, or 3 in a sample; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the polypeptide.

30 54. A method of diagnosing a thyroid gland related pathological condition or a susceptibility to a thyroid gland related pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the polypeptide of Claims 13, 14, or 15 or the polypeptide encoded by the nucleic acid molecule of Claims 1, 2, or 3 in a sample; and

5 (b) diagnosing a thyroid gland related pathological condition or a susceptibility to a thyroid gland related pathological condition based on the presence or amount of expression of the polypeptide.

10 55. A device, comprising:

(a) a membrane suitable for implantation; and

(b) cells encapsulated within said membrane, wherein said cells secrete a polypeptide of Claims 13, 14, or 15, and wherein said membrane is permeable to
15 said protein and impermeable to materials detrimental to said cells.

56. A method of identifying a compound which binds to a polypeptide comprising:

20 (a) contacting the polypeptide of Claims 13, 14, or 15 with a compound; and

(b) determining the extent of binding of the polypeptide to the compound.

25 57. A method of modulating levels of a polypeptide in an animal comprising administering to the animal the nucleic acid molecule of Claims 1, 2, or 3.

30 58. A transgenic non-human mammal comprising the nucleic acid molecule of Claims 1, 2, or 3.

59. A heterodimer of human β 10 polypeptide and

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human $\alpha 2$ polypeptide.

60. A naturally occurring variant of the $\alpha 2/\beta 10$ heterodimer of Claim 59.

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61. A vector comprising nucleic acid molecules encoding human $\beta 10$ polypeptide and human $\alpha 2$ polypeptide.

10 62. A host cell comprising the vector of Claim 61.

63. The host cell of Claim 62 that is a prokaryotic cell.

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64. The host cell of Claim 62 that is a eukaryotic cell.

20 65. A process of producing an $\alpha 2/\beta 10$ heterodimer comprising culturing the host cell of Claim 62 under suitable conditions to express the $\alpha 2/\beta 10$ heterodimer, and optionally isolating the $\alpha 2/\beta 10$ heterodimer from the culture.

25 66. A heterodimer produced by the process of Claim 65.

30 67. A process for determining whether a compound modulates $\alpha 2/\beta 10$ heterodimer activity or production comprising exposing a cell according to Claim 62 to the compound, and measuring $\alpha 2/\beta 10$ heterodimer activity or production in said cell.

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68. An antibody produced by immunizing an animal with a human $\alpha 2/\beta 10$ heterodimer.

69. An antibody or fragment thereof that
5 specifically binds the $\alpha 2/\beta 10$ heterodimer of claim 59 or naturally occurring variant thereof.

70. The antibody of Claim 69 that is a monoclonal antibody.
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71. A hybridoma that produces the monoclonal antibody of claim 70 which is specific to an $\alpha 2/\beta 10$ heterodimer.

72. A method of detecting or quantitating the
15 amount of an $\alpha 2/\beta 10$ heterodimer using the antibody of claim 69.

73. A selective binding agent or fragment thereof
20 that specifically binds at least one of the following:

- (a) the $\alpha 2/\beta 10$ heterodimer of claim 59;
- (b) a fragment of the $\alpha 2/\beta 10$ heterodimer of claim 59; and
- 25 (c) a naturally occurring variant of (a) or (b).

74. The selective binding agent of Claim 73 that is an antibody or fragment thereof.
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75. The selective binding agent of Claim 73 that is a humanized antibody.

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76. The selective binding agent of Claim 73 that is a human antibody or fragment thereof.

77. The selective binding agent of Claim 73 that is a polyclonal antibody or fragment thereof.

78. The selective binding agent of Claim 73 that is a monoclonal antibody or fragment thereof.

79. The selective binding agent of Claim 73 that is a chimeric antibody or fragment thereof.

80. The selective binding agent of Claim 73 that is a CDR-grafted antibody or fragment thereof.

81. The selective binding agent of Claim 73 that is an anti-idiotypic antibody or fragment thereof.

82. The selective binding agent of Claim 73 which is a variable region fragment.

83. The variable region fragment of Claim 82 which is a Fab or a Fab' fragment.

84. A selective binding agent or fragment thereof comprising at least one complementarity determining region with specificity for a human $\alpha 2/\beta 10$ heterodimer.

85. The selective binding agent of Claim 73 which is bound to a detectable label.

86. The selective binding agent of Claim 73 which antagonizes an $\alpha 2/\beta 10$ heterodimer biological activity.

87. A method for treating, preventing, or

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ameliorating a disease, condition, or disorder comprising administering to a patient an effective amount of an $\alpha 2/\beta 10$ heterodimer according to claim 59, or a selective binding agent that specifically binds said heterodimer or fragment or naturally occurring variant thereof.

88. A method for treating, preventing, or ameliorating a thyroid gland related disease, condition, or disorder comprising administering to a patient an effective amount of an $\alpha 2/\beta 10$ heterodimer according to claim 59, or a selective binding agent that specifically binds said heterodimer or fragment or naturally occurring variant thereof.

89. A composition comprising the heterodimer of claim 59, or a naturally occurring variant of said heterodimer, or a fragment of said heterodimer, or a selective binding agent of any of the foregoing, and a pharmaceutically acceptable formulation agent.

90. The composition of Claim 89 wherein the pharmaceutically acceptable formulation agent is a carrier, adjuvant, solubilizer, stabilizer, or anti-oxidant.

91. A method of modulating levels of an $\alpha 2/\beta 10$ heterodimer in an animal comprising administering to the animal the nucleic acid molecule of Claims 1, 2, or 3.

92. The heterodimer of Claim 59 or naturally occurring variant thereof which is covalently modified with a water-soluble polymer.

93. The heterodimer of Claim 92 wherein the water-soluble polymer is selected from the group consisting of polyethylene glycol, monomethoxy-polyethylene glycol, dextran, cellulose, poly-(N-vinyl pyrrolidone) polyethylene glycol, propylene glycol homopolymers, polypropylene oxide/ethylene oxide co-polymers, polyoxyethylated polyols, and polyvinyl alcohol.

94. A fusion polypeptide comprising the heterodimer of Claim 59 or naturally occurring variant thereof fused to a heterologous amino acid sequence.

95. The fusion polypeptide of Claim 94 wherein the heterologous amino acid sequence is an IgG constant domain or fragment thereof.

96. A method of diagnosing a pathological condition or a susceptibility to a pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the heterodimer of Claim 59 or naturally occurring variant thereof; and

(b) diagnosing a pathological condition or a susceptibility to a pathological condition based on the presence or amount of expression of the heterodimer.

97. A method of diagnosing a thyroid gland related pathological condition or a susceptibility to a thyroid gland related pathological condition in a subject comprising:

(a) determining the presence or amount of expression of the heterodimer of Claim 59 or naturally occurring variant thereof; and

(b) diagnosing a thyroid gland related

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pathological condition or a susceptibility to a thyroid gland related pathological condition based on the presence or amount of expression of the heterodimer.

5 98. A device, comprising:

(a) a membrane suitable for implantation; and

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10 (b) cells encapsulated within said membrane, wherein said cells secrete an $\alpha 2/\beta 10$ heterodimer of Claim 59 or naturally occurring variant thereof, and wherein said membrane is permeable to said heterodimer and impermeable to materials detrimental to said cells.

99. A method of identifying a compound which binds to a heterodimer comprising:

15 (a) contacting the heterodimer of Claim 59 or naturally occurring variant thereof with a compound; and

20 (b) determining the extent of binding of the heterodimer to the compound.